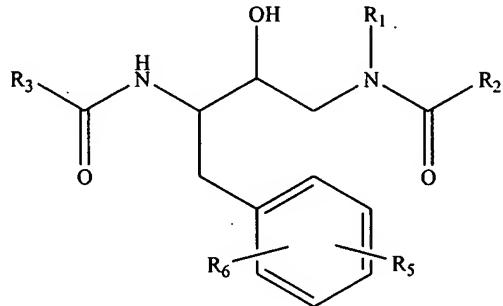


**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1           1 (currently amended): A method for modulating the processing of an amyloid  
2 precursor protein (APP), said method comprising contacting a composition containing said APP  
3 with an aspartyl protease inhibitor having the general formula:  
4



(I)

5           wherein:

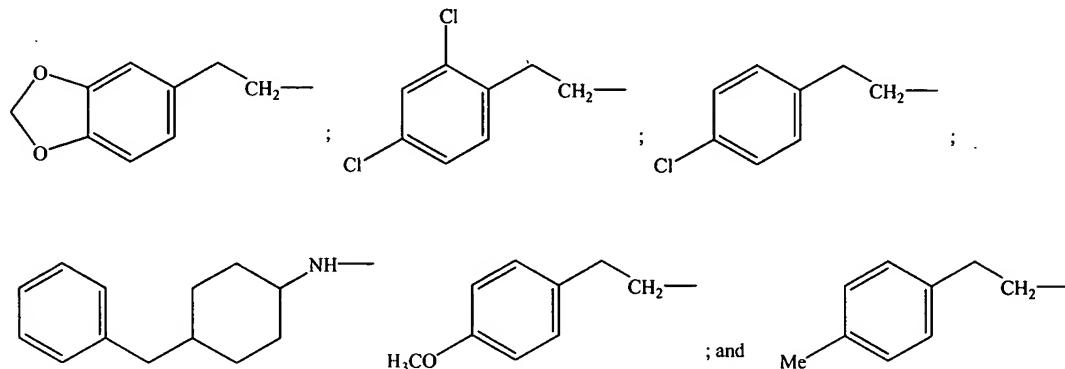
6           R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are members independently selected from the group consisting of  
7           alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted  
8           arylalkyl, aryloxyalkyl, substituted aryloxyalkyl, heteroaryl, substituted  
9           heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heterocycles,  
10           substituted heterocycles, heterocyclicalkyl and substituted  
11           heterocyclicalkyl; and

12           R<sub>5</sub> and R<sub>6</sub> are independently selected from the group consisting of hydrogen,  
13           halogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl,  
14           substituted arylalkyl, aryloxyalkyl and substituted aryloxyalkyl; or R<sub>5</sub> and  
15           R<sub>6</sub> and the carbons to which they are bound join to form an optionally

17 substituted carbocyclic or heterocyclic fused ring system having a total of  
18 9- or 10-ring atoms within said fused ring system.

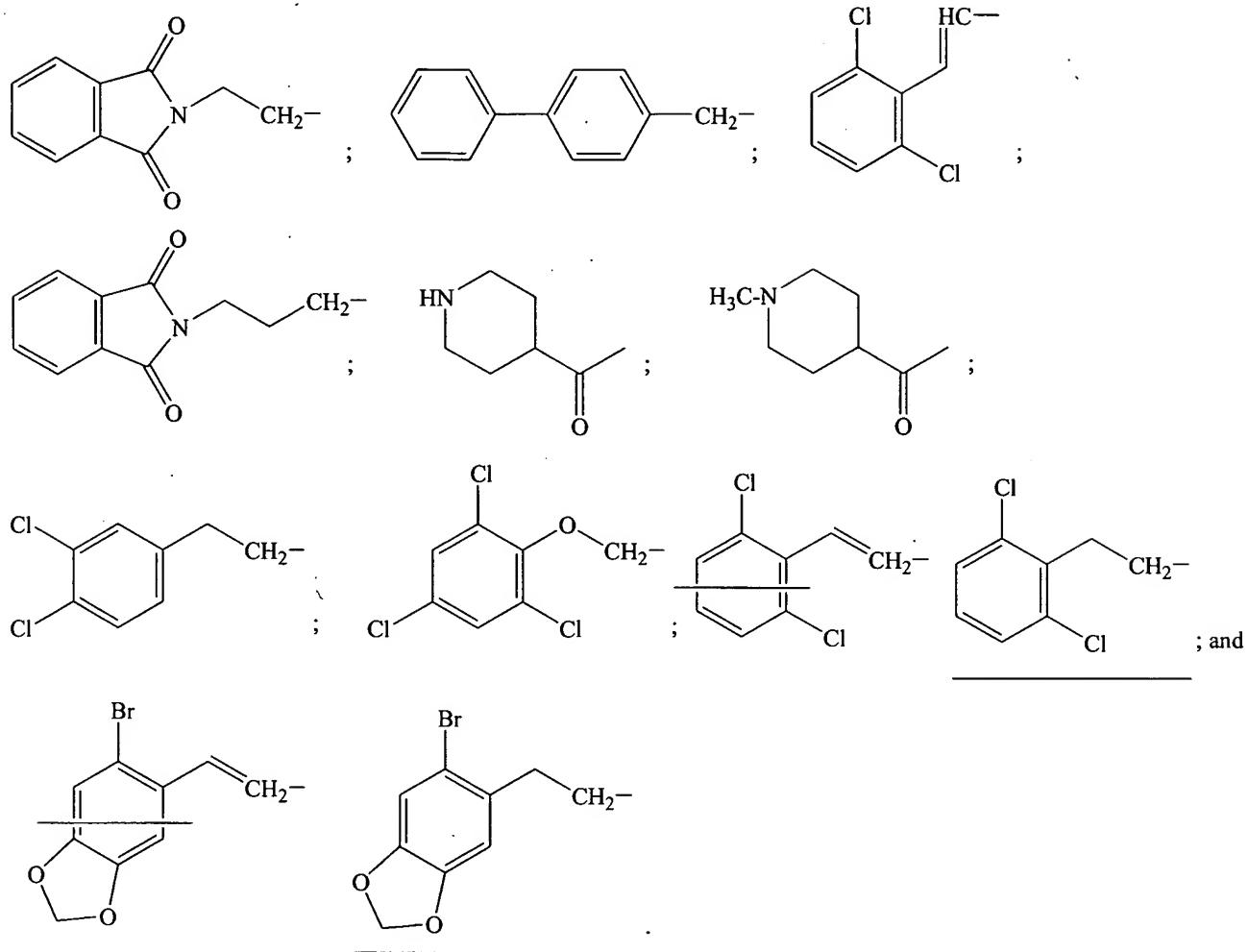
2 (original): The method according to claim 1, wherein:  
R<sub>1</sub> is a member selected from the group consisting of substituted alkylaryl, substituted aryl, substituted alkyl and substituted heterocyclic groups.

1 3 (original): The method according to claim 2, wherein:  
2 R<sub>1</sub> is a member selected from the group consisting of:



4 (original): The method according to claim 1, wherein:  
R2 is a member selected from the group consisting of substituted alkyl,  
and substituted heterocyclic groups.

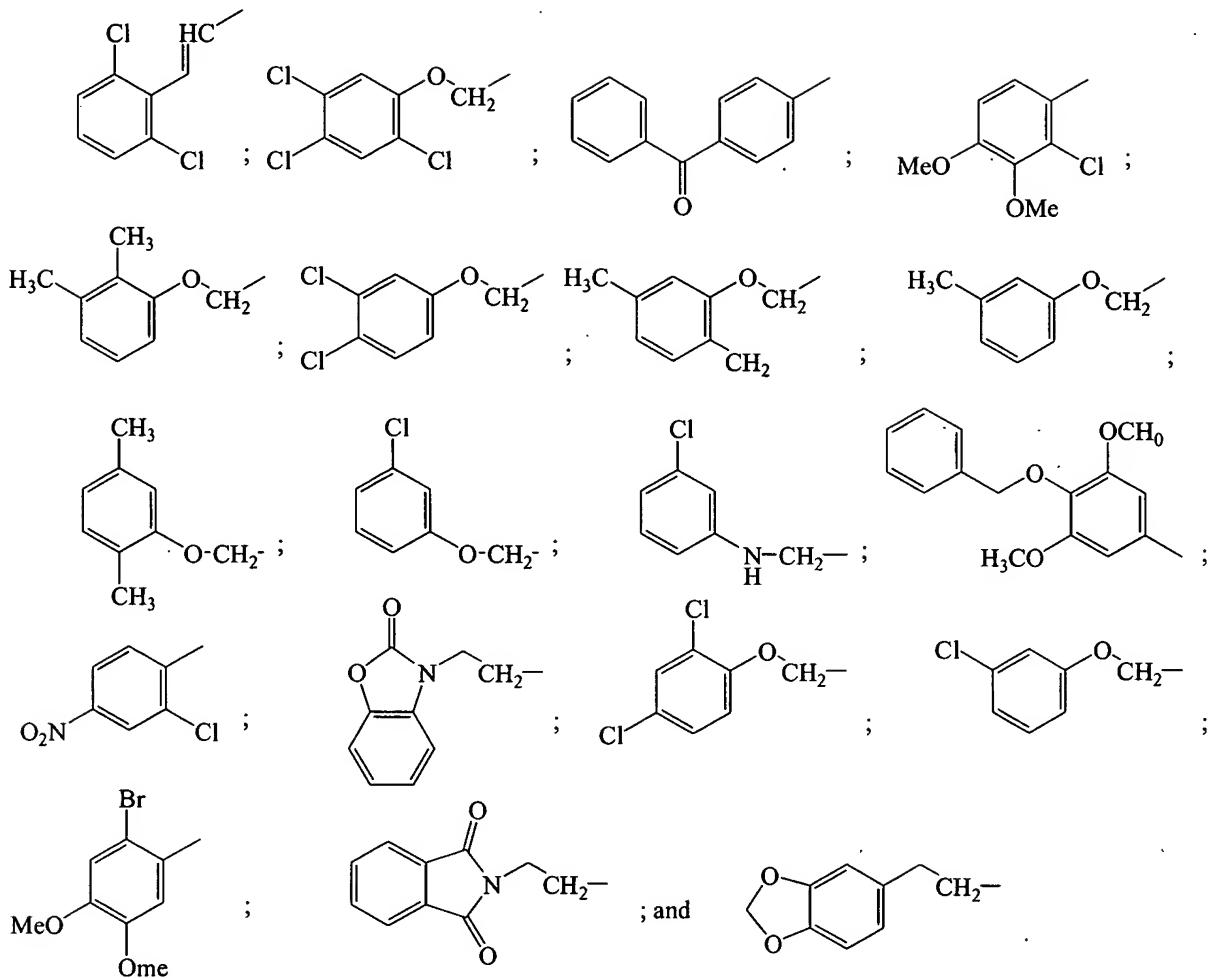
5 (currently amended): The method according to claim 4, wherein R<sub>2</sub> is a member selected from the group consisting of:



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1                   6 (original): The method according to claim 1, wherein:  
2                   R<sub>3</sub> is a member selected from the group consisting of substituted alkyl and  
3                   substituted aryl groups.

1                   7 (original): The method according to claim 6, wherein R<sub>3</sub> is a member selected  
2                   from the group consisting of:

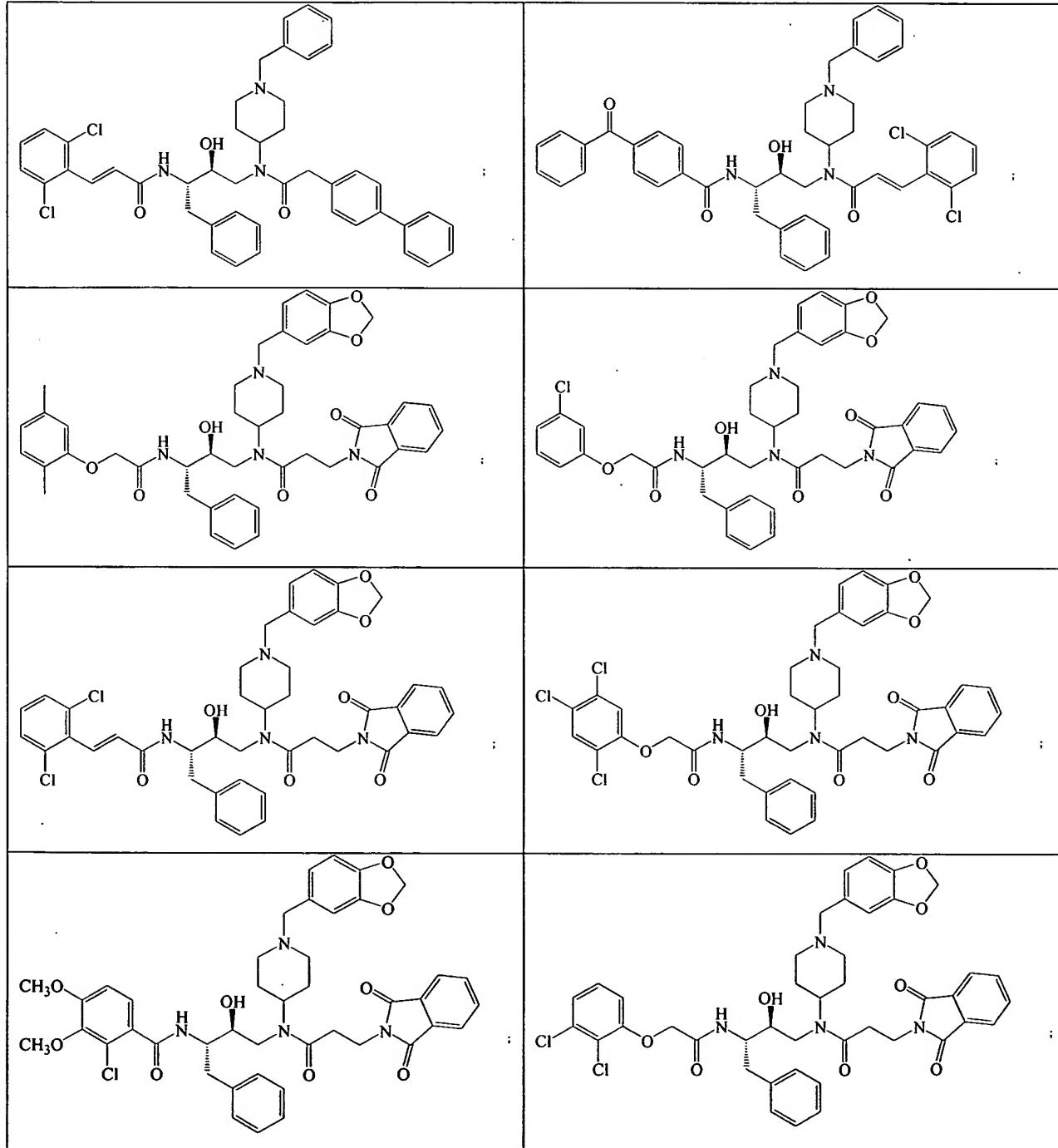


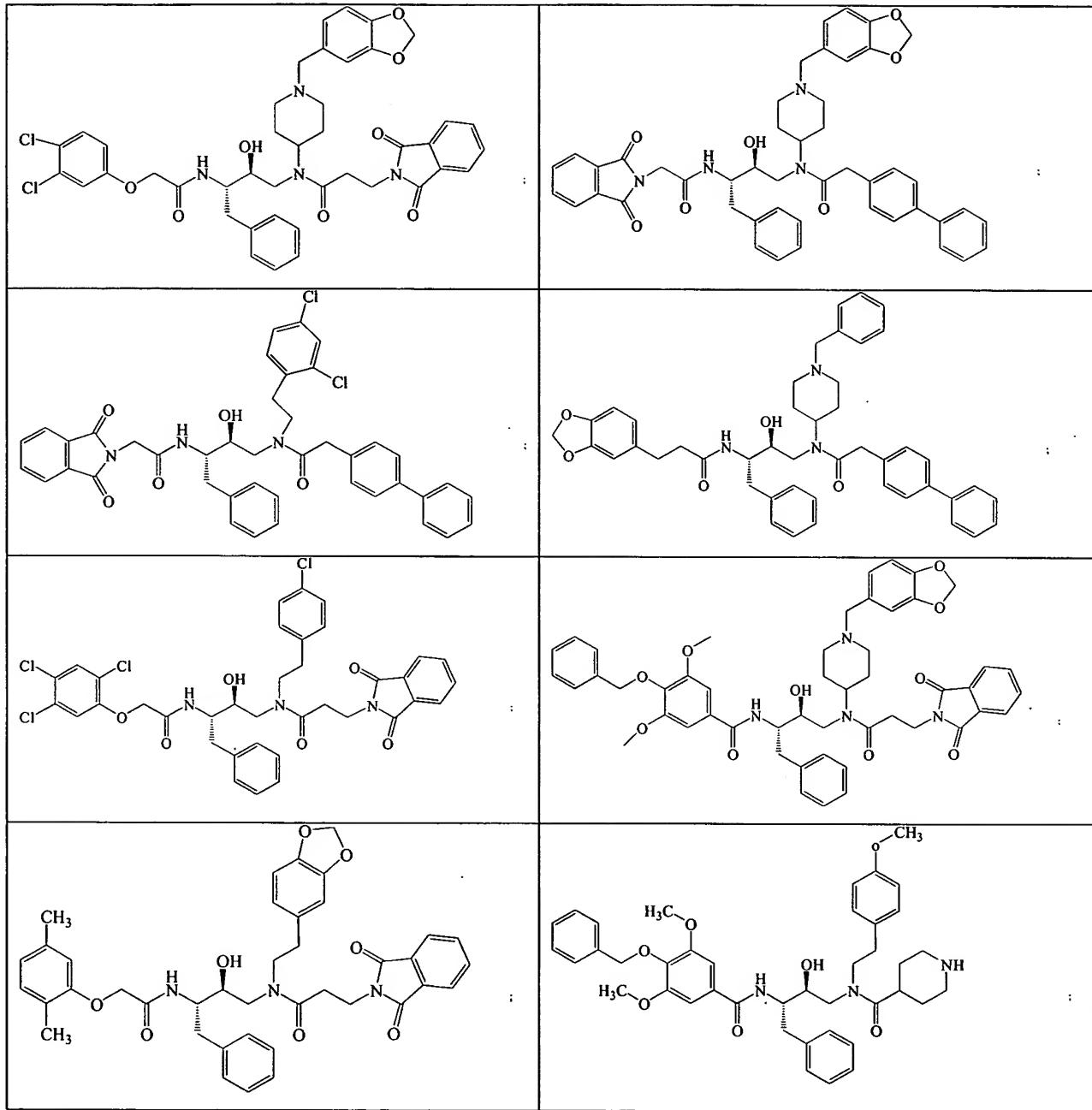
1                   8 (original): The method according to claim 1, wherein R<sub>5</sub> and R<sub>6</sub> and the  
2                   carbons to which they are bound form an optionally substituted naphthalene ring.

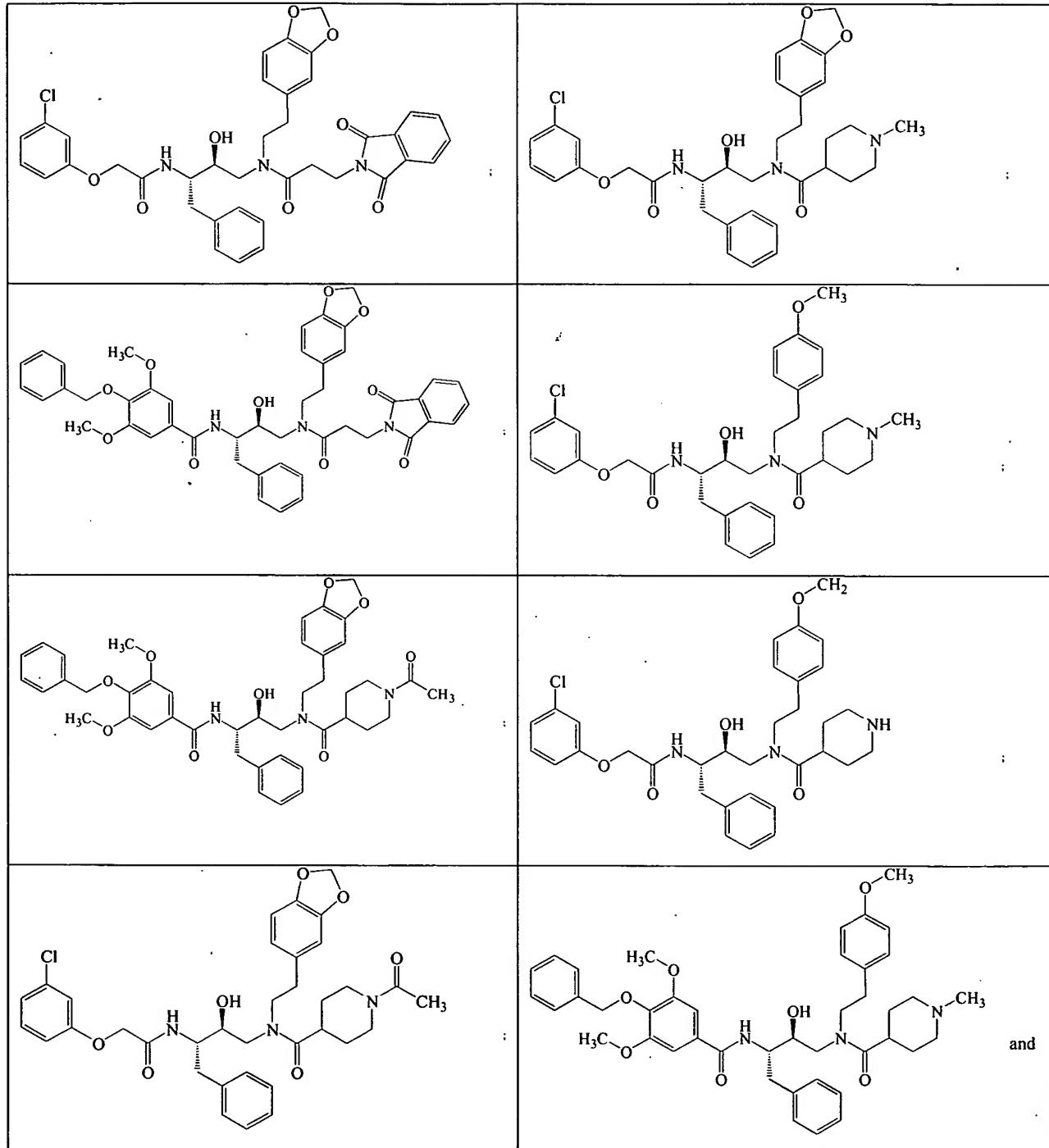
1                   9 (original): The method according to claim 1, wherein R<sub>5</sub> and R<sub>6</sub> are both  
2                   hydrogen.

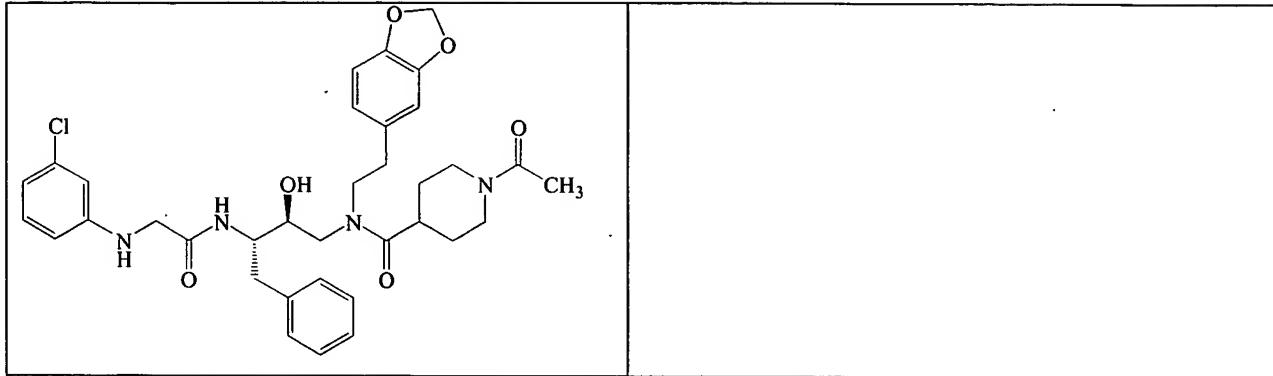
1                   10 (original): The method in accordance with claim 1, wherein R<sub>5</sub> is hydrogen  
2                   and R<sub>6</sub> is meta or para to R<sub>5</sub> and is a member selected from the group consisting of halogen,  
3                   alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl and  
4                   substituted aryloxyalkyl.

1                   11 (original): The method according to claim 1, wherein said aspartyl protease  
2                   inhibitor is a member selected from the group consisting of:





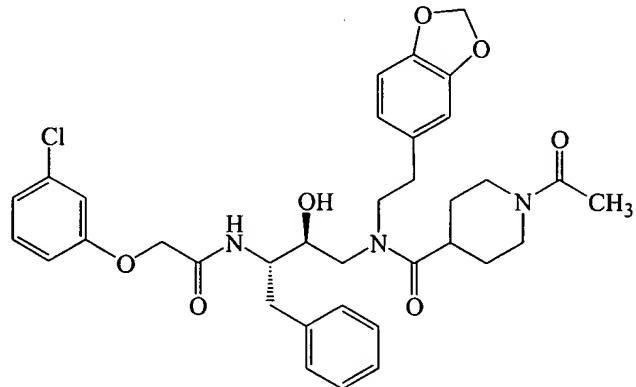




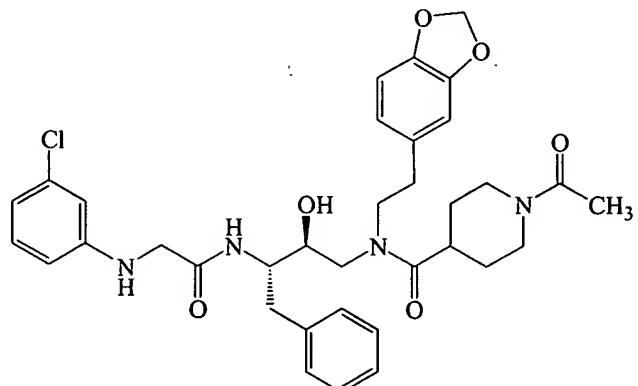
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4

1           12 (original): The method according to claim 1, wherein said aspartyl protease  
2           inhibitor is a member selected from the group consisting of:



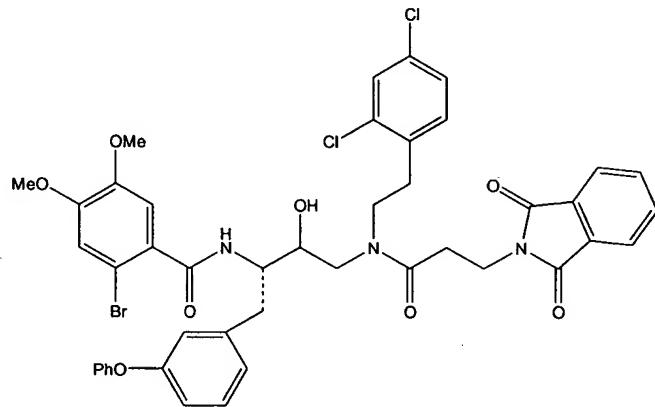
3           and



4

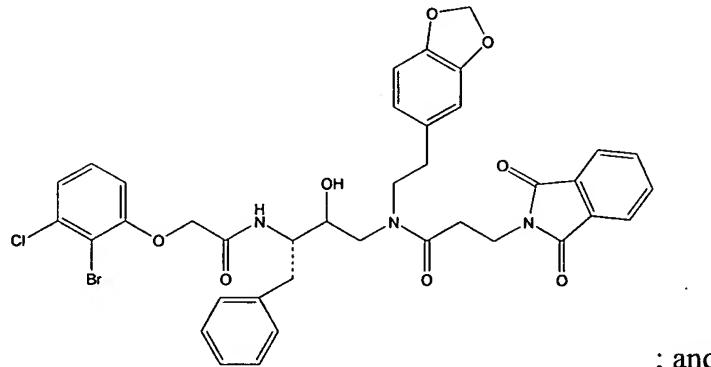
1                   13 (currently amended): The method in accordance with claim 1, wherein said  
2 aspartyl protease inhibitor is a member selected from the group consisting of ~~CEL5-A, CEL5-G~~  
3 and ~~EA-1, which are illustrated in FIG. 12~~

4                   CEL5-A having the following structure:



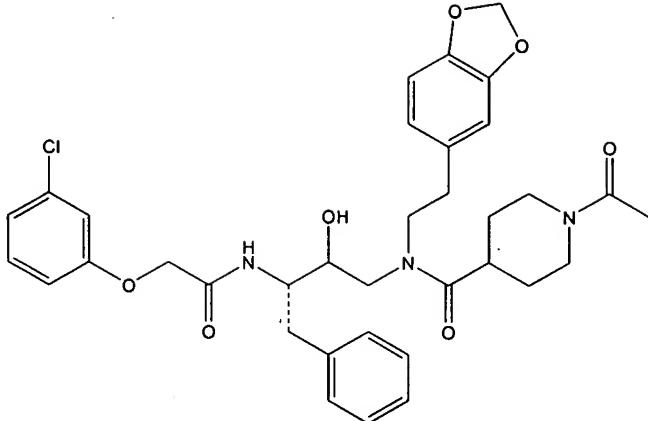
5                   ;

6                   CEL5G having the following structure:



7                   ; and

8                   EA 1 having the following structure:



9

1 14 (original): The method in accordance with claim 1, wherein said composition  
2 is a body fluid.

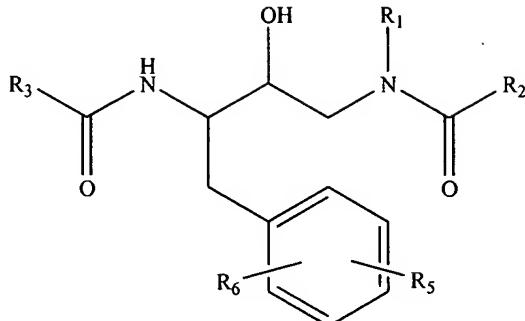
1 15 (currently amended): The method in accordance with claim [[13,]] 14,  
2 wherein said body fluid is cerebral spinal fluid.

1 16 (original): The method in accordance with claim 1, whereby formation of  
2 amyloidogenic A $\beta$  peptides (A $\beta$ ) is decreased compared to the amount formed in the absence of  
3 said aspartyl protease inhibitor.

1 17 (original): The method in accordance with claim 1, whereby formation of  $\alpha$ -  
2 sAPP is increased compared to the amount formed in the absence of said aspartyl protease  
3 inhibitor.

1 18 (original): The method in accordance with claim 1, wherein the modulation is  
2 effected by modulating the activity of cathepsin D.

1 19 (currently amended): A method for modulating the processing of a tau-  
2 protein ( $\tau$ -protein), said method comprising contacting a composition containing said  $\tau$ -protein  
3 with an aspartyl protease inhibitor having the **general formula**:



4 (I)

5 wherein:

6 R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are members independently selected from the group consisting of  
7 alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted  
8 arylalkyl, aryloxyalkyl, substituted aryloxyalkyl, heteroaryl, substituted  
9 heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heterocycles,  
10 substituted heterocycles, heterocyclicalkyl and substituted  
11 heterocyclicalkyl; and

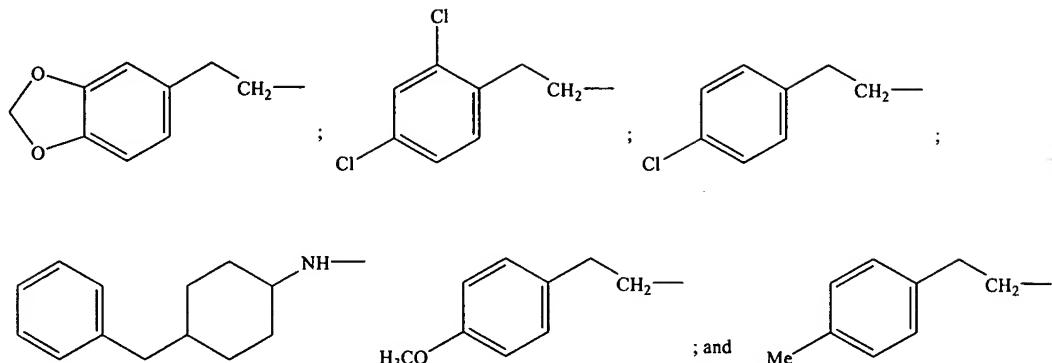
12 R<sub>5</sub> and R<sub>6</sub> are independently selected from the group consisting of hydrogen,  
13 halogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl,  
14 substituted arylalkyl, aryloxyalkyl and substituted aryloxyalkyl; or R<sub>5</sub> and  
15 R<sub>6</sub> and the carbons to which they are bound join to form an optionally  
16 substituted carbocyclic or heterocyclic fused ring system having a total of  
17 9- or 10-ring atoms within said fused ring system.

1 20 (original): The method according to claim 19, wherein:

2 R<sub>1</sub> is a member selected from the group consisting of substituted alkylaryl,  
3 substituted aryl, substituted alkyl and substituted heterocyclic groups.

1 21 (original): The method according to claim 20, wherein:

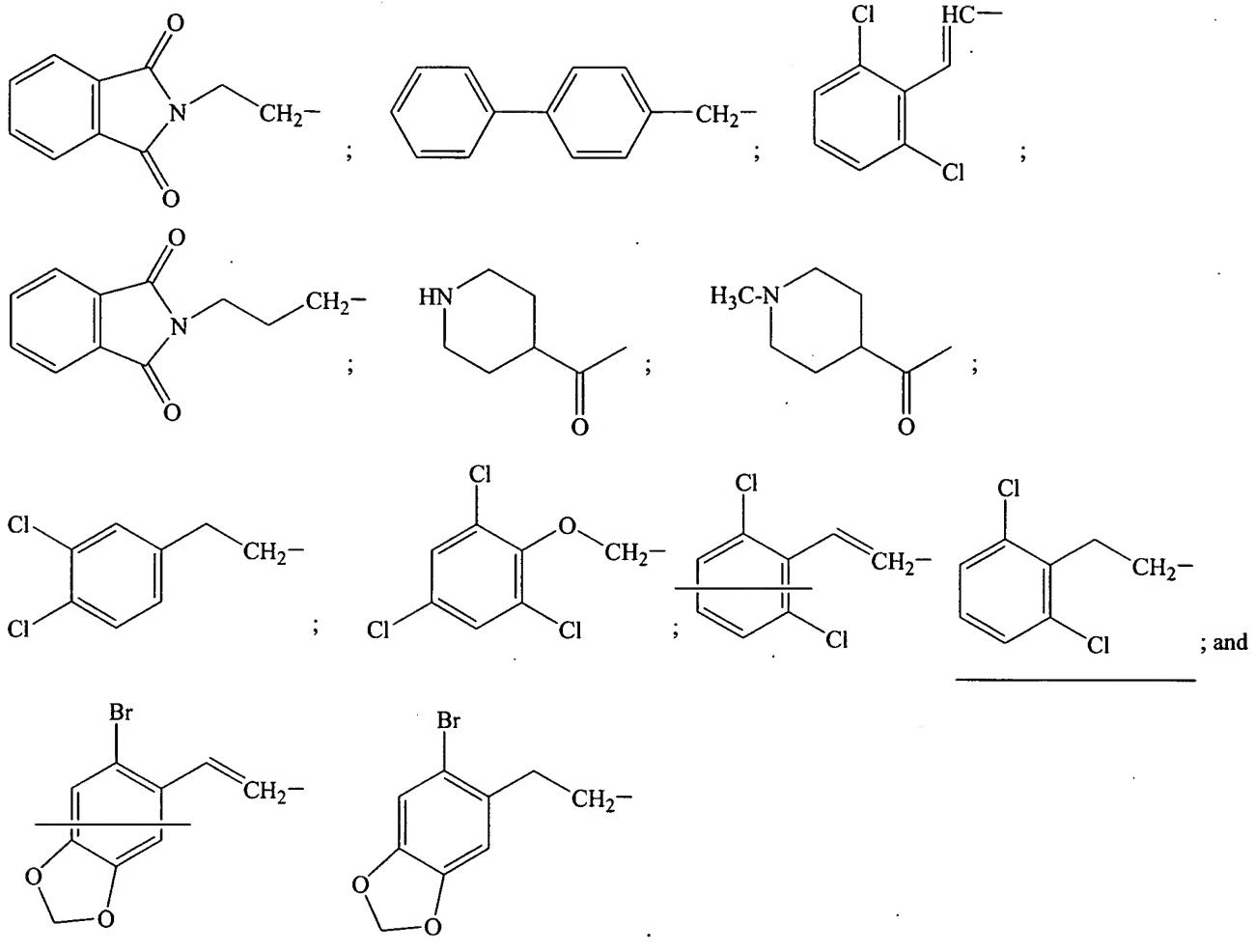
2 R<sub>1</sub> is a member selected from the group consisting of:



3

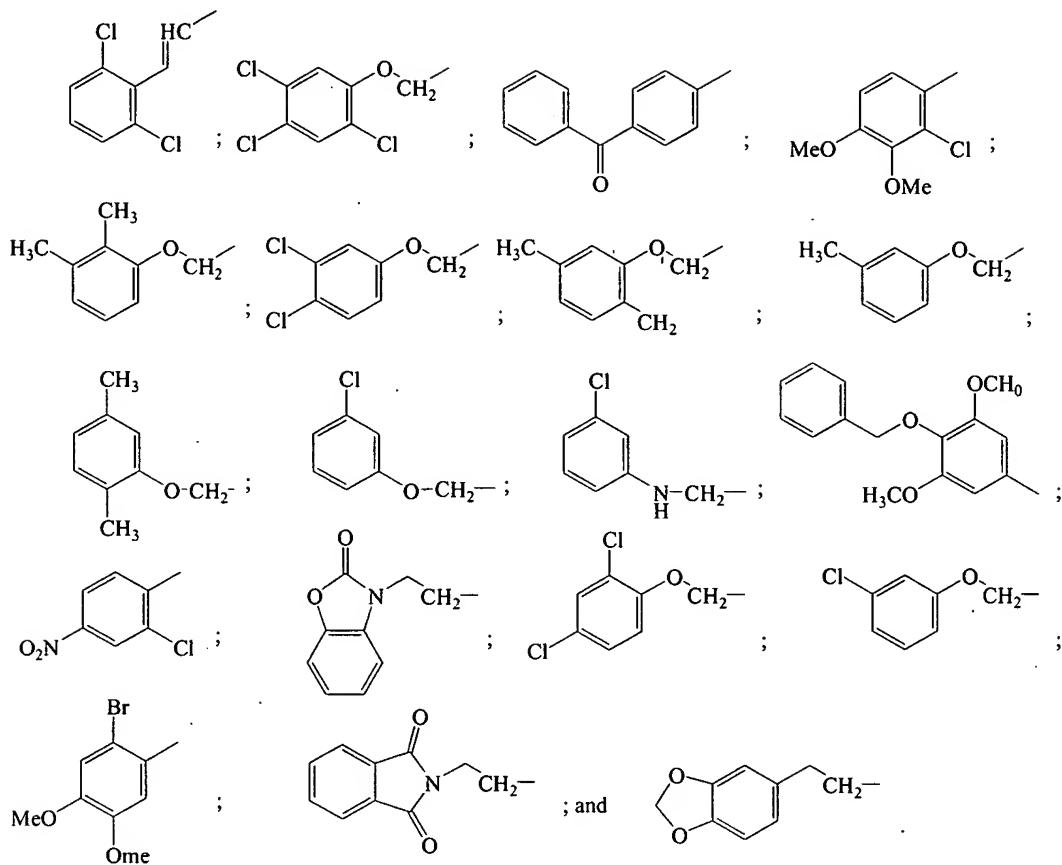
1                   22 (original): The method according to claim 19, wherein:  
2                   R<sub>2</sub> is a member selected from the group consisting of substituted alkyl,  
3                   heterocyclic and substituted heterocyclic groups.

1                   23 (currently amended): The method according to claim 22, wherein R<sub>2</sub> is a  
2                   member selected from the group consisting of:



3  
4  
1 24 (original): The method according to claim 19, wherein:  
2 R<sub>3</sub> is a member selected from the group consisting of substituted alkyl and  
3 substituted aryl groups.

1  
2 25 (original): The method according to claim 24, wherein R<sub>3</sub> is a member  
selected from the group consisting of:

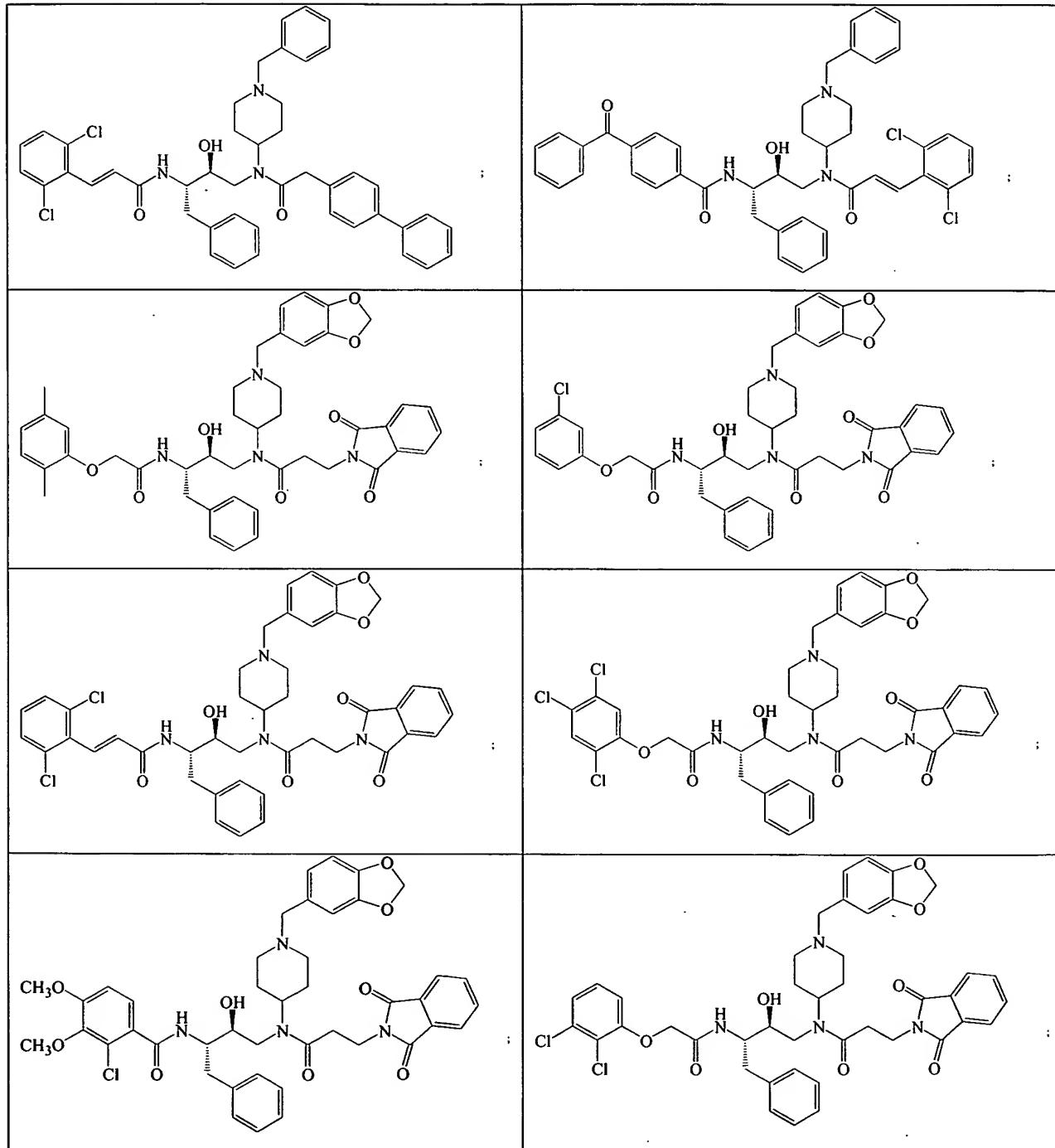


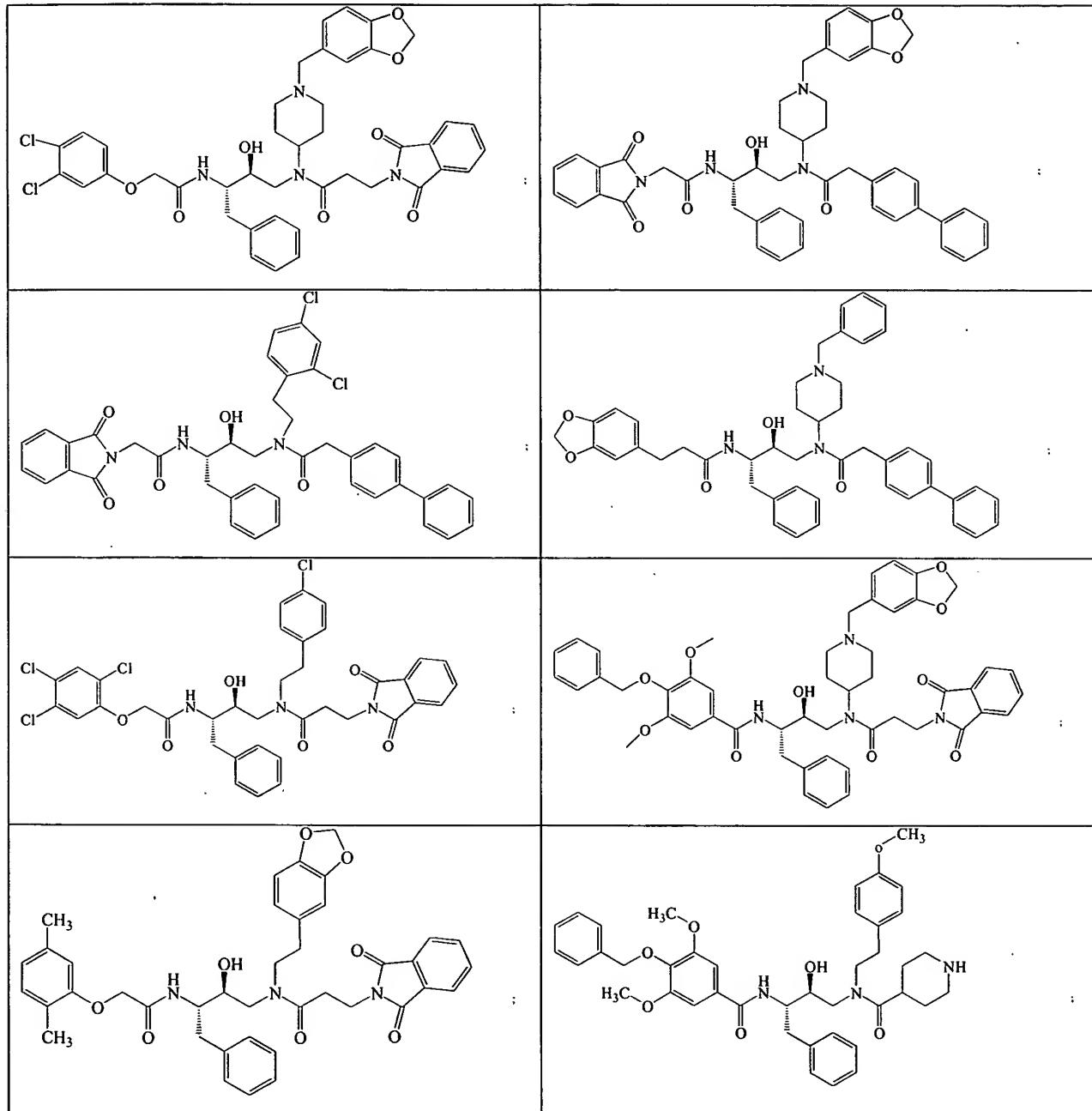
1           26 (original): The method according to claim 19, wherein R<sub>5</sub> and R<sub>6</sub> and the  
2           carbons to which they are bound form an optionally substituted napthalene ring.

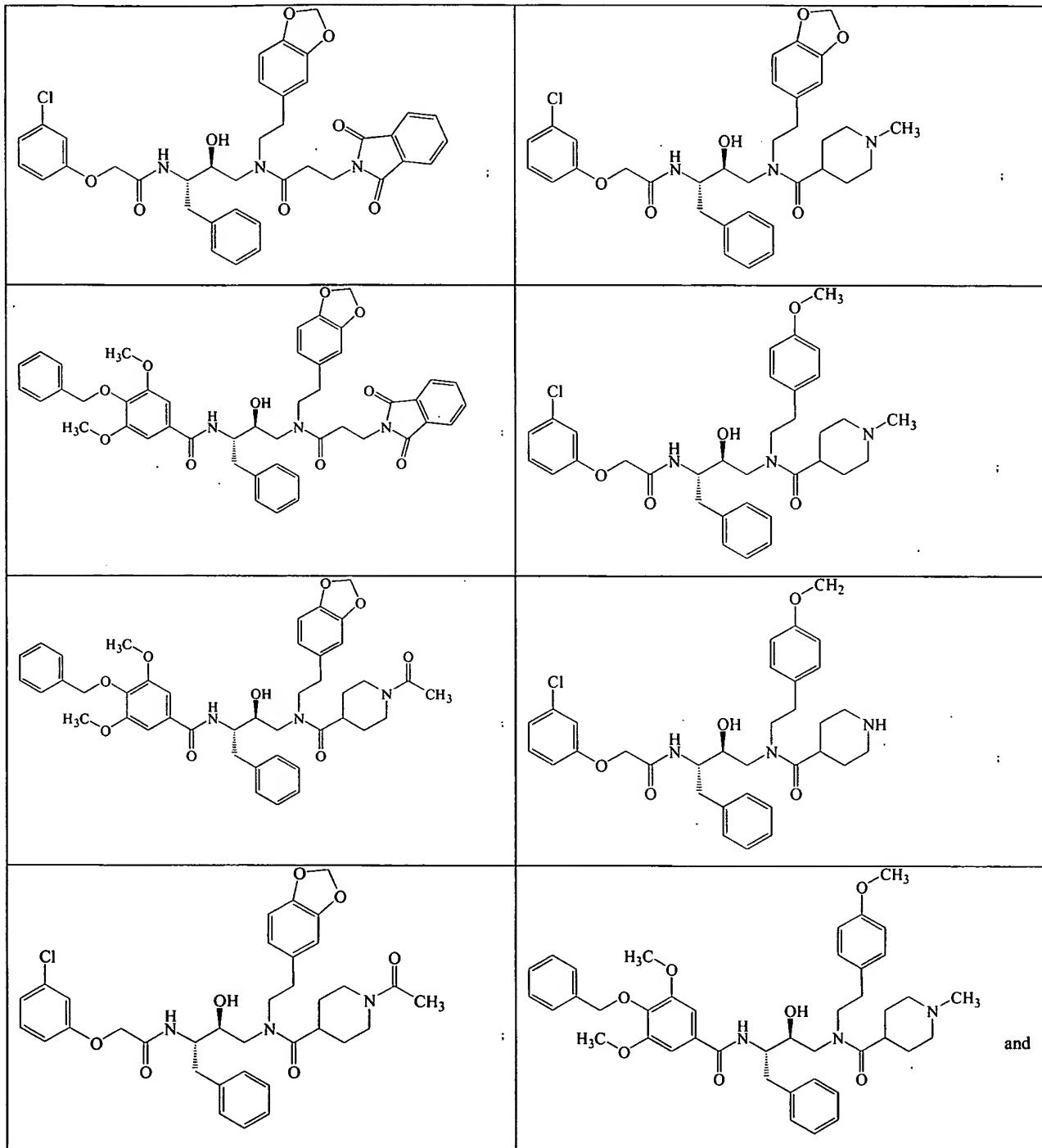
1           27 (original): The method according to claim 19, wherein R<sub>5</sub> and R<sub>6</sub> are both  
2           hydrogen.

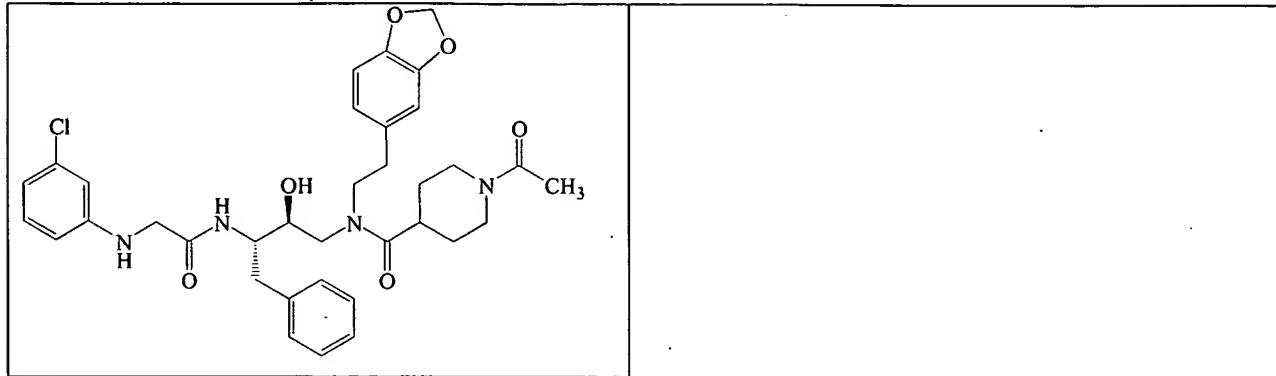
1           28 (original): The method in accordance with claim 19, wherein R<sub>5</sub> is hydrogen  
2           and R<sub>6</sub> is meta or para to R<sub>5</sub> and is a member selected from the group consisting of halogen,  
3           alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl and  
4           substituted aryloxyalkyl.

1           29 (original): The method according to claim 19, wherein said aspartyl protease  
2           inhibitor is a member selected from the group consisting of:



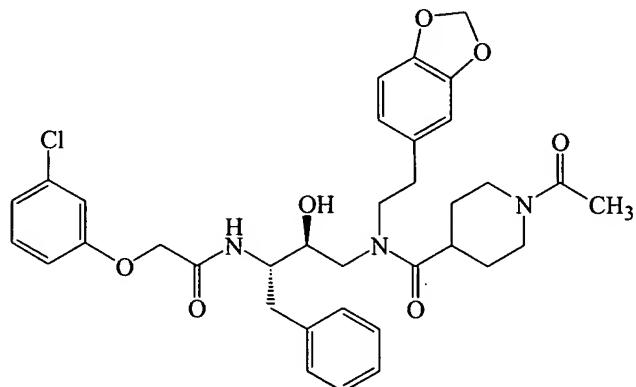




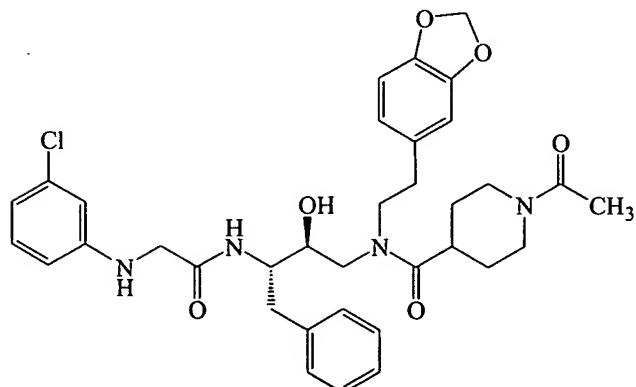


3

1                   30 (original): The method according to claim 19, wherein said aspartyl protease  
2                   inhibitor is a member selected from the group consisting of:



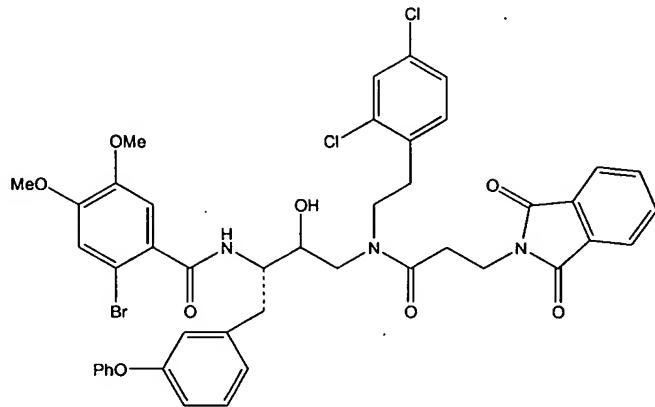
3                   and



4

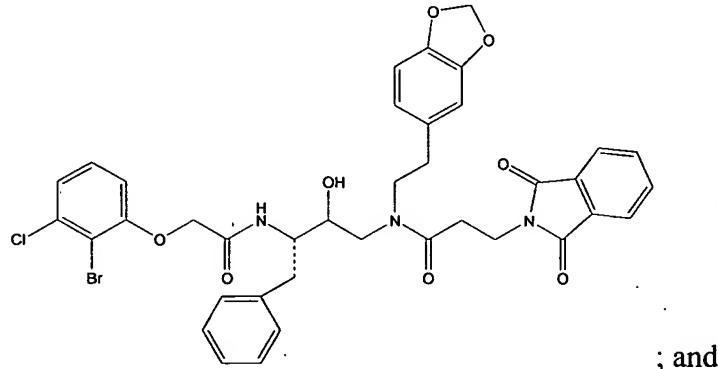
1                   31 (currently amended): The method in accordance with claim 19, wherein said  
2 aspartyl protease inhibitor is a member selected from the group consisting of ~~CEL5-A, CEL5-G~~  
3 and EA-1, which are illustrated in FIG. 12

4                   CEL5-A having the following structure:



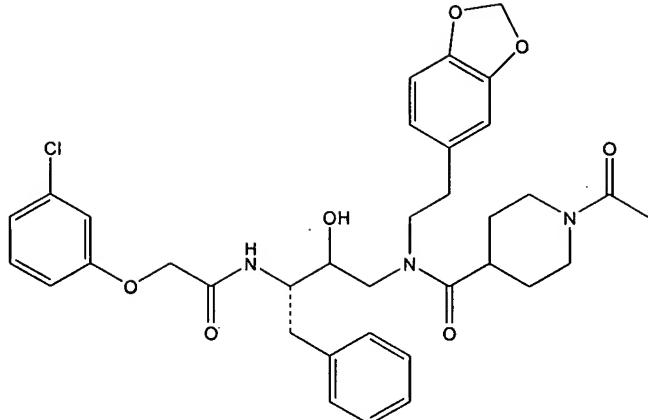
5                   ;

6                   CEL5G having the following structure:



7                   ; and

8                   EA 1 having the following structure:



9

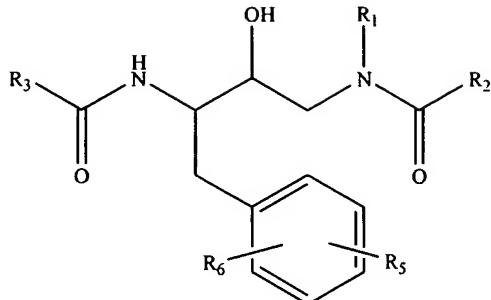
1           32 (original): The method in accordance with claim 19, wherein said  
2 composition is a body fluid.

1           33 (currently amended): The method in accordance with claim [[31,]] 32,  
2 wherein said body fluid is cerebral spinal fluid.

1           34 (original): The method in accordance with claim 19, whereby formation of  $\tau$ -  
2 fragments is decreased compared to the amount formed in the absence of said aspartyl protease  
3 inhibitor.

1           35 (original): The method in accordance with claim 19, wherein the modulation  
2 is effected by modulating the activity of cathepsin D.

1           36 (currently amended): A method for treating a neurodegenerative disorder,  
2 said method comprising: administering to a mammal a therapeutically effective amount of an  
3 aspartyl protease inhibitor having the **general** formula:



4 (I)

5 wherein:

6 R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are members independently selected from the group consisting of  
7 alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted  
8 arylalkyl, aryloxyalkyl, substituted aryloxyalkyl, heteroaryl, substituted  
9 heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heterocycles,  
10 substituted heterocycles, heterocyclicalkyl and substituted  
11 heterocyclicalkyl; and

12 R<sub>5</sub> and R<sub>6</sub> are independently selected from the group consisting of hydrogen,  
13 halogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl,  
14 substituted arylalkyl, aryloxyalkyl and substituted aryloxyalkyl; or R<sub>5</sub> and  
15 R<sub>6</sub> and the carbons to which they are bound join to form an optionally  
16 substituted carbocyclic or heterocyclic fused ring system having a total of  
17 9- or 10-ring atoms within said fused ring system; and  
18 a pharmaceutically acceptable carrier,

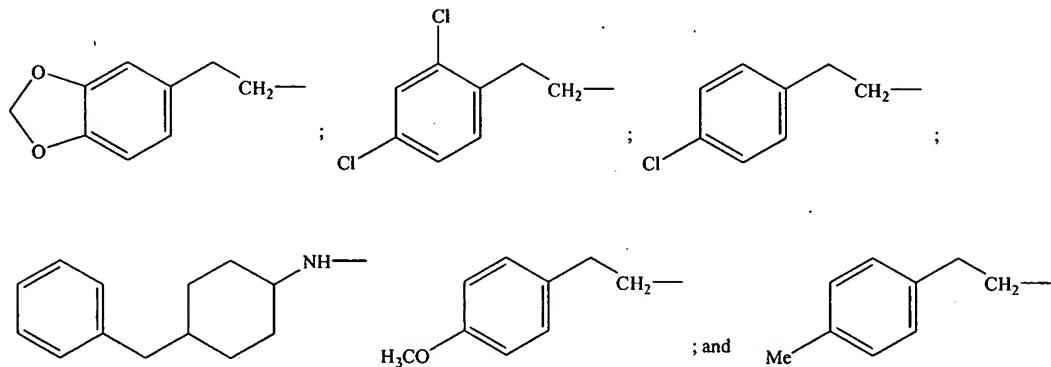
19 wherein: said neurodegenerative disorder is characterized by the accumulation of amyloid  
20 plaques or by the accumulation of the accumulation of  $\tau$ -fragments.

37-38 (canceled)

1 39 (original): The method in accordance with claim 36, wherein said  
2 neurodegenerative disorder is a member selected from the group consisting of Alzheimer's  
3 disease, Parkinson's disease, cognition defects, Downs Syndrome, cerebral hemorrhage with  
4 amyloidosis, dementia and head trauma.

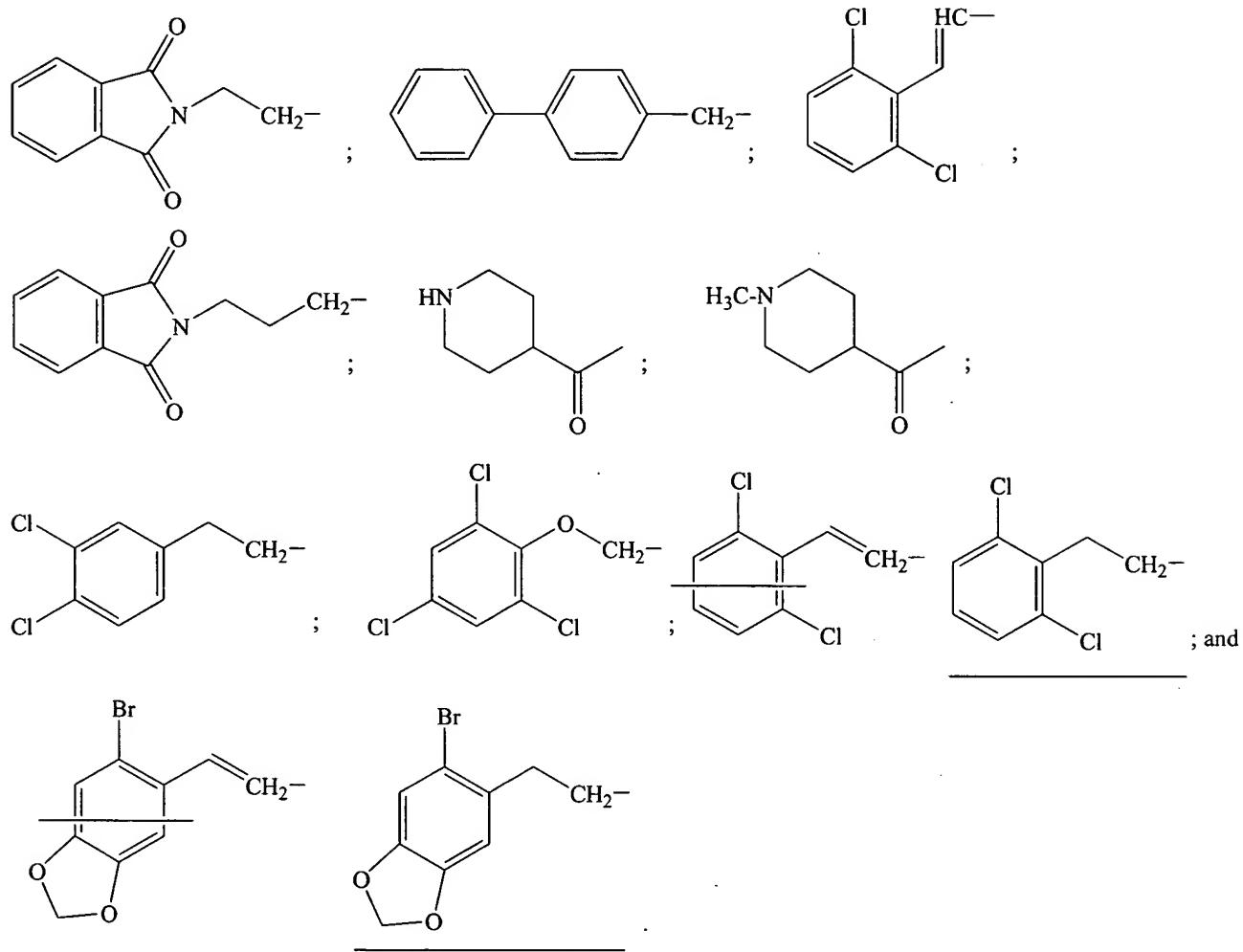
1           40 (original): The method according to claim 36, wherein:  
2           R<sub>1</sub> is a member selected from the group consisting of substituted alkylaryl,  
3           substituted aryl, substituted alkyl and substituted heterocyclic groups.

1           41 (original): The method according to claim 40, wherein:  
2           R<sub>1</sub> is a member selected from the group consisting of:



1           42 (original): The method according to claim 36, wherein:  
2           R<sub>2</sub> is a member selected from the group consisting of substituted alkyl,  
3           heterocyclic and substituted heterocyclic groups.

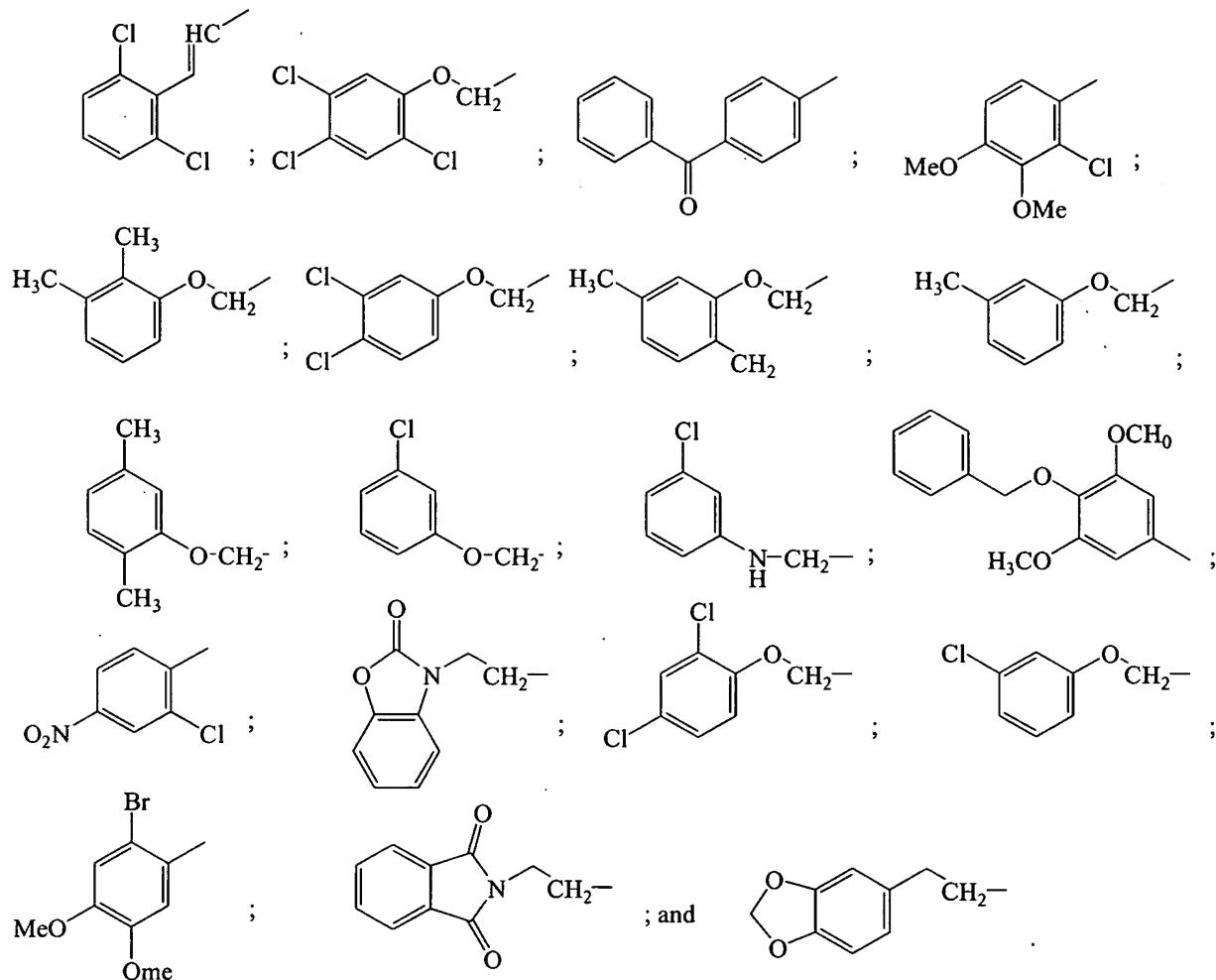
1           43 (currently amended): The method according to claim 42, wherein R<sub>2</sub> is a  
2           member selected from the group consisting of:



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1                   44 (original): The method according to claim 36, wherein:  
2                   R<sub>3</sub> is a member selected from the group consisting of substituted alkyl and  
3                   substituted aryl groups.

1                   45 (original): The method according to claim 44, wherein R<sub>3</sub> is a member  
2                   selected from the group consisting of:

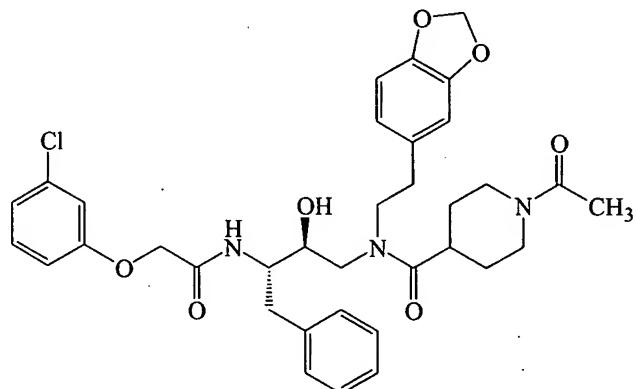


1                   46 (original): The method according to claim 36, wherein R<sub>5</sub> and R<sub>6</sub> and the  
2                   carbons to which they are bound form an optionally substituted naphthalene ring.

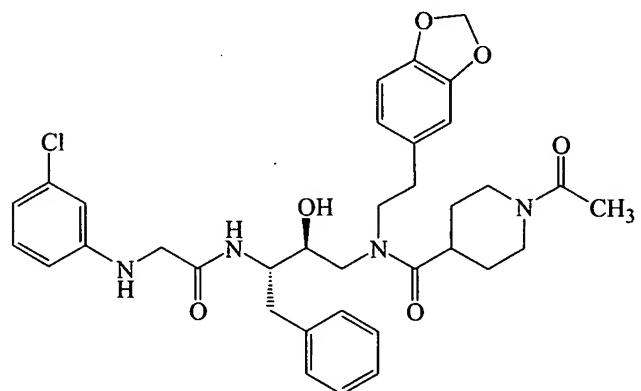
1                   47 (original): The method according to claim 36, wherein R<sub>5</sub> and R<sub>6</sub> are both  
2                   hydrogen.

1                   48 (original): The method in accordance with claim 36, wherein R<sub>5</sub> is hydrogen  
2                   and R<sub>6</sub> is meta or para to R<sub>5</sub> and is a member selected from the group consisting of halogen,  
3                   alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl and  
4                   substituted aryloxyalkyl.

1 49 (original): The method in accordance with claim 36, wherein said aspartyl  
2 protease inhibitor is a member selected from the group consisting of:



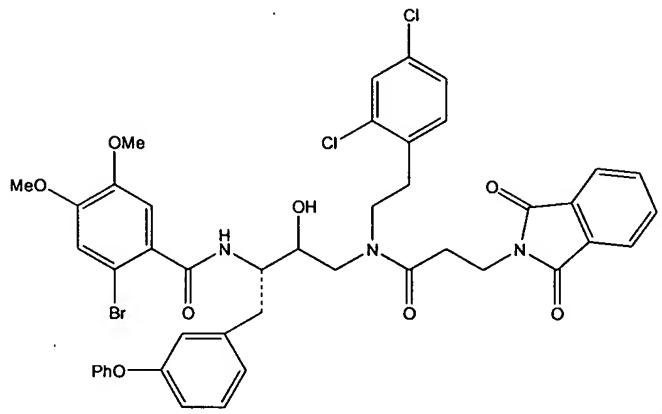
and



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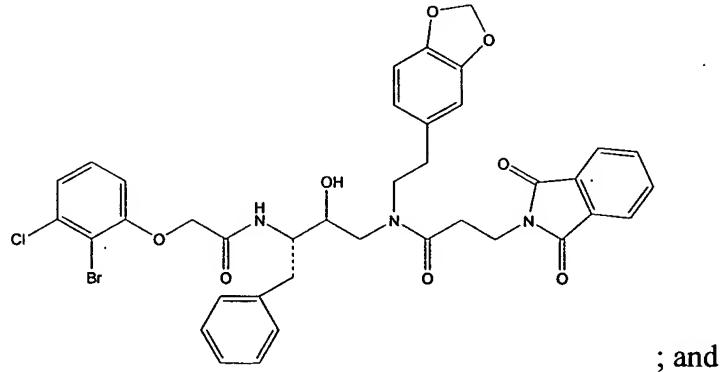
50 (currently amended): The method in accordance with claim 36, wherein said aspartyl protease inhibitor is a member selected from the group consisting of ~~CEL5-A, CEL5-G and EA-1, which are illustrated in FIG. 12~~

CEL5-A having the following structure:



;

CEL5G having the following structure:



; and

EA 1 having the following structure:

Appl. No. 10/774,262  
Amdt. dated June 2, 2005  
Reply to Office Action of December 2, 2004

PATENT

